Original Article

Desmopressin Acetate Before Percutaneous Ultrasound-Guided Kidney Biopsy in Patients with Renal Failure – Is it Really Beneficial?

Leena Jose, Anupma Kaul, Dharmendra Bhadauria, Ravi Kushwaha, Raghu Nandan[1], Hira Lal[1], Narayan Prasad, Manas Ranjan Behera, Manas Ranjan Patel

Departments of Nephrology and [1]Radiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Abstract

Introduction: The most common complication of percutaneous renal biopsy is bleeding, which can be seen in up to one-third of cases. The aim of this study was to evaluate the effect of prebiopsy administration of intranasal desmopressin acetate in reducing the incidence of biopsy-related bleeding complications in patients with significant renal dysfunction who underwent renal biopsy. **Methods:** This was a retrospective, observational study of percutaneous native renal biopsies performed at our center from July 2014 to June 2018. Bleeding complication rates of patients with renal failure (estimated glomerular filtration rate [eGFR] <30 mL/minute/1.73 m^2) who received desmopressin and those who did not receive desmopressin were compared. **Results:** Desmopressin administration before renal biopsy in patients with eGFR <30 mL/minute/1.73 m^2 was associated with a significant reduction of bleeding complications (major and minor together; $P = 0.025$) and no significant reduction in major complications ($P = 0.616$) or intervention rates ($P = 0.251$) when compared with a group that did not receive desmopressin. **Conclusions:** While prebiopsy intranasal desmopressin use was associated with a significant reduction of overall bleeding complications including major and minor complications, there was no reduction in the rate of other major complications and interventions.

Keywords: *Complications, desmopressin, kidney biopsy, renal failure*

Introduction

Kidney biopsy is an essential tool for the diagnosis, adequate treatment, and prognosis of many primary and secondary renal diseases. The technique for percutaneous liver biopsy was adapted to the kidney by Nils Alwall and further refined by Karl and Muehrcke in 1954 who used the modified Vim–Silverman needle for kidney biopsy.[1,2] Currently, the use of real-time ultrasound and automated spring-loaded biopsy gun is standard practice.

The most common complication of renal biopsy is bleeding. Other complications include pain, arteriovenous fistulas, page kidney and chronic hypertension, perirenal soft tissue infection, and rarely injury of abdominal organs and urinoma if the urinary tract is punctured. The risk of bleeding is higher with lower glomerular filtration rate (GFR), vasculitis, uncontrolled hypertension, female gender, and advanced age.[3,4] The risk of minor bleeding episodes including self-limiting gross hematuria or small hematomas that did not need any blood transfusion or intervention ranges from 17% to 33% in a large meta-analysis of 9,474 kidney biopsies, whereas major complications, including hemorrhage requiring transfusion, angiographic intervention, nephrectomy, or death, have been reported in only around 2% to 8% of renal biopsies.[5,6]

Various measures to minimize the bleeding complications of kidney biopsy such as the use of desmopressin acetate, recombinant activated factor VII, reptilase, and vitamin K1; stopping antiplatelet agents; and controlling blood pressure have been tried.[4]

The characteristic hemostatic defects in patients with renal failure are prolonged bleeding time and platelet dysfunction. Desmopressin has been shown to be effective in improving the bleeding time or *in vitro* tests of platelet dysfunction in at least one-half of patients and appears to act by increasing the release of large factor VIII: von Willebrand factor multimers from endothelial cells and

How to cite this article: Jose L, Kaul A, Bhadauria D, Kushwaha R, Nandan R, Lal H, *et al.* Desmopressin acetate before percutaneous ultrasound-guided kidney biopsy in patients with renal failure – Is it really beneficial? Indian J Nephrol 2022;32:430-4.

Received: 10-12-2020
Revised: 01-09-2021
Accepted: 14-09-2021
Published: 11-05-2022

Address for correspondence:
Dr. Anupma Kaul, Professor, Department of Nephrology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.
E-mail: anupmaneph@gmail.com

Access this article online

Website: www.indianjnephrol.org

DOI: 10.4103/ijn.IJN_553_20

Quick Response Code:

may also increase the platelet membrane glycoprotein expression.[7,8] Desmopressin may be given intravenously or subcutaneously at a dose of 0.3 μg/kg (in 50 mL of saline over 15–30 minutes if intravenously), or intranasally at a dose of 3 μg/kg. DDAVP nasal spray (desmopressin acetate) is a synthetic analog of the natural pituitary hormone 8-arginine vasopressin (antidiuretic hormone [ADH]). One milliliter (0.1 mg) of intranasal DDAVP has an antidiuretic activity of about 400 IU; 10 μg of desmopressin acetate is equivalent to 40 IU. The half-life of DDAVP increases in patients with significant renal impairment.

A randomized controlled trial on the role of subcutaneous desmopressin acetate in low-risk patients undergoing kidney biopsy with creatinine <1.5 mg/dL published by Manno *et al.*[9] showed a significant reduction of minor complications such as hematomas. Another multicenter pilot study by Peters *et al.*[10] using subcutaneous desmopressin acetate (dose 0.3 μg/kg) in patients with impaired renal function (serum creatinine above 150 μmol/L) found lower major and overall complication rates in the desmopressin acetate arm.

A study on the role of low-dose intranasal DDAVP for uremic bleeding in 11 children on maintenance hemodialysis thrice a week found that the bleeding time decreased with 30 μg intranasal desmopressin dose. They hypothesized that DDAVP may be improving the platelet function at such low doses by increasing platelet serotonin uptake and ATP (adenosine triphosphate) release.[11]

Radhakrishnan *et al.*[12] did not find a statistically significant reduction in bleeding for patients receiving preprocedural DDAVP in patients with GFR <60 mL/minute/1.73 m^2 in their study. However, in patients with an estimated glomerular filtration rate (eGFR) <15 mL/minute/1.73 m^2, there was a trend toward a benefit for the role of DDAVP, but the numbers were small.

The aim of this study was to compare the rate of all bleeding complications (major and minor) in patients who received prebiopsy intranasal desmopressin as compared to those who did not.

Materials and Methods

This was a retrospective, single-center, study conducted at Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, India, between July 2014 and June 2018. Patients who underwent percutaneous renal biopsies in this period at our center formed the subject of study. Of these, consecutive patients with renal failure and eGFR < 30 mL/minute/1.73 m^2 were included in the study. Patients' demographic data, indications for biopsy, laboratory reports, and clinical and hemodynamic parameters were collected from the electronic medical records and their individual files. All patients included had normal coagulation parameters (bleeding time was not measured) and platelet count >100 × 10^3/μL. Anticoagulation and antiplatelet drugs were routinely withdrawn before kidney biopsy at our center 7 days before the biopsy.

Exclusion criteria included deranged coagulation parameters or thrombocytopenia, small-sized kidneys, multiple bilateral cysts, horseshoe kidney, hydronephrosis, pyelonephritis, perirenal abscess, uncontrolled blood pressure, and patients who did not give consent. Patients whose intranasal route was compromised due to nasal congestion, discharge, severe atrophic rhinitis, impaired consciousness, and patients whose serum sodium level was <130 mmol/L were not given desmopressin.

Patients who underwent kidney biopsy from 2014 to 2016 when desmopressin was not routinely used at our center and patients who could not be given desmopressin due to local complications or hyponatremia were included in the "no desmopressin" group.

Intranasal desmopressin was used before 307 biopsies, whereas 125 patients did not receive desmopressin. The dose of intranasal desmopressin used was 40 μg puffs in each nostril, given twice – the first dose an hour before and the second one 15 minutes before the biopsy (cumulative dose of desmopressin = 160 μg).

The kidney biopsies were performed using a percutaneous technique with real-time ultrasonography imaging and needle tracking guide (Ultra-pro II™ Needle guide, Civco, Iowa, USA) on a Toshiba, Japan, Xario model SSA-660a, with a 3.75-MHz curvilinear probe. All biopsies were performed by a nephrologist and a trainee nephrologist. The American Society of Diagnostic and Interventional Nephrology requires nephrologists to have completed each procedure as a primary performer a minimum of 25 times to be certified, and the nephrology trainees at our institute are adequately trained and have performed kidney biopsies that exceed this number many times over. The biopsies were taken using automated spring-loaded devices (Bard Peripheral Vascular Inc., USA, BARD® Max-core™ disposable core biopsy needle) with 18 gauge, and 16-cm long needle with a penetration depth of 22 mm and a sample notch of 18 mm.

All patients were advised to lay supine in the bed with a compression bandage over the biopsy site for at least 6 hours with overnight bed rest and close monitoring of urine for gross hematuria, blood pressure, and pulse rate. Hemoglobin and hematocrit were measured after 6 hours and 24 hours of the biopsy. A screening ultrasound was done immediately after the biopsy by the nephrologist performing the procedure. Repeat ultrasound or computed tomography was done by a radiologist if any signs or symptoms of a bleeding complication such as a significant decrease in hemoglobin, hypotension, flank pain, or hematuria were present.

Patient-related information was collected from the hospital informatics system. This study was approved by the

Institutional Ethics Committee, and prior informed consents were obtained from all patients.

Outcome parameters

Primary outcome parameters

The primary outcome parameters were as follows:

- Incidence of post–renal biopsy bleeding complications in the desmopressin and no desmopressin groups.
- Overall complications (including minor and major) and major complications were separately studied in desmopressin and no desmopressin groups.
- Minor complications were defined as perinephric hematoma and gross hematuria that resolved spontaneously without intervention and did not require a blood transfusion.
- Major complications included a significant decline in hemoglobin level requiring blood transfusions, arteriovenous fistula, or renal arterial pseudoaneurysm requiring radiological intervention such as angiography, gel foam transarterial embolization or coiling, nephrectomy, and death.

Secondary outcome parameters were the requirement for blood transfusion, blood pressure, and length of hospital stay. Data on each patient's age, gender, pre-biopsy and post-biopsy hemoglobin, intervention done if any, diagnosis, and the timing of complications were also collected.

Statistical analysis

Unpaired Student's *t*-test was used for comparative analysis between the two groups. Pearson's Chi-square test or Fisher exact test was employed to analyze categorical data as appropriate. A P value < 0.05 was considered significant. Statistical Package for the Social Sciences, Version 22 (SPSS 22, IBM Chicago, USA) was used for statistical analyses.

Results

Baseline demographics

A total of 2,844 percutaneous native renal biopsies were done at our center from July 2014 to June 2018. A total of 432 patients (275 men and 157 women) with eGFR <30 mL/minute/1.73 m^2 who underwent native kidney biopsy in this period were included in the study. The demographic and bleeding parameters in the desmopressin and no desmopressin groups are compared in Table 1. The mean age of these patients was 39.1 ± 15.3 years, and all renal biopsies were done as an inpatient procedure. Desmopressin was not used in 125 patients, and 307 patients were given intranasal desmopressin as per protocol. More than half of the patients in either group received hemodialysis before the biopsy. Indications for the renal biopsy were a rapidly progressive renal failure in 162 (37.5%), chronic kidney disease in 110 (25.5%) patients, acute kidney injury (AKI) in 115 (26.6%) patients, and nephrotic syndrome with AKI in 45 (10.4%) patients.

Primary outcome measures

Out of the 432 (14.81%) patients, 64 had a bleeding complication and 17 (3.93%) of them had a major bleeding complication needing either blood transfusions or intervention. The group given intranasal desmopressin had a significantly lower number of all bleeding complications (major and minor) compared with the no desmopressin use (38 of 307, 12.37% vs. 26 of 125, 20.80%; $P = 0.025$). The relative risk of all bleeding complications with desmopressin use was 0.595 (95% confidence interval [CI] 0.378–0.936). However, desmopressin use did not significantly decreased the risk of major bleeding complications (13 of 307, 4.23% vs. 4 of 125, 3.20%; $P = 0.62$). Thirteen patients of 432 (3.01%) needed intervention such as gel foam embolization or coiling. There was no significant difference between the two groups in the number of small hematomas found on immediate post-biopsy ultrasound screening (30 of 307, 9.8% vs. 19 of 125, 15.2% $P = 0.11$). The need for interventions was not found to be different in two groups (10 of 307, 3.26% vs. 3 of 125, 2.40%; $P = 0.64$). None of the patients needed nephrectomy in our study. Table 2 shows the bleeding complication rates and management of these patients.

Secondary outcome measures

There was no significant difference between the two groups with respect to the need for blood transfusions (23 of 307, 7.5% vs. 15 of 125, 12%, $P = 0.13$), systolic, diastolic, or mean arterial pressures.

Desmopressin use was not associated with a decrease in the length of stay in the hospital (14.3 vs. 14.6 days, $P = 0.74$). However, the length of hospital stay was longer in patients with major bleeding complications (14.2 vs. 20.3 days; $P = 0.007$). As the study included patients with eGFR <30 mL/minute/1.73 m^2 exclusively, many of the patients required dialysis and treatment of the underlying renal disease (including immunosuppression induction) after the biopsy, and the long length of stay across all groups of patients reflects that.

In relation to the time to detection of bleeding complications in our study is concerned, a total of 52 (81.25%) patients had bled in the first 24 hours, eight (12.50%) patients from 24 hours to 7 days, and four (6.25%) patients presented with bleeding after 7 days of the biopsy. One patient in desmopressin group with bleeding complication died due to a hospital acquired infection. There were no deaths directly due to a bleeding complication.

Discussion

In our single-center, retrospective study of patients with eGFR <30 mL/minute/1.73m^2 who underwent percutaneous kidney biopsy under ultrasound guidance, prebiopsy intranasal administration of desmopressin was associated with a significantly lower overall rate of bleeding

Table 1: Demographic and coagulation parameters of desmopressin and no desmopressin groups

	Desmopressin group (*n*=307)	No desmopressin group (*n*=125)	*P*
Age (years)	39.2±15.4	38.9±15.5	0.82
Gender (male:female)	193:114	82:43	
Hemoglobin (g/dL)	9.33±1.33	9.63±1.38	0.037
Platelet count	219.31±88.05	228.41±93.58	0.34
aPTT (seconds)	28.41±3.47	28.28±3.19	0.72
INR	1.12±0.13	1.12±0.14	0.86
Systolic blood pressure (in mmHg)	134.3±7.7	134.7.7	0.92
Diastolic blood pressure (in mmHg)	83.3±7.5	84.5±7.9	0.13
Mean arterial pressure (in mmHg)	100.3±6.7	101.1±7.1	0.25
Creatinine (mg/dL)	6.07±1.63	5.86±1.63	0.22
Estimated GFR (mL/minute/1.73 m^2)	10.89±3.71	11.62±4.22	0.09
Number of biopsy passes	2.25±0.47	2.27±0.46	0.62
HD dependent	162 (52.8%)	68 (54.4%)	0.84
Length of stay in hospital (days)	14.3±8.9	14.7±9.6	0.74

aPTT=activated partial thromboplastin time; GFR=glomerular filtration rate; HD=hemodialysis

Table 2: Bleeding complication rates and outcomes in desmopressin and no desmopressin groups

	Desmopressin group (*n*=307)	No desmopressin group (*n*=125)	*P*
All bleeding complications	38 (12.38%)	26 (20.80%)	0.025
Hematoma on immediate post-biopsy ultrasound screen	30 (9.77%)	19 (15.2%)	0.11
Major bleeding complications	13 (4.23%)	4 (3.2%)	0.62
Interventions	10 (3.26%)	3 (2.4%)	0.25
Post-biopsy blood transfusion requirement	23 (7.49%)	15 (12%)	0.13
Length of stay in hospital (days)	8.9	9.6	0.742

complications (12.37% vs. 20.80%; $P = 0.025$). The decrease in minor bleeding complications in our study is consistent with the randomized controlled trial by Manno *et al.*,[9] where parenteral desmopressin was used in low-risk kidney biopsy patients with similar findings. This RCT did not have major bleeding complications in any patient of either group. A recent study by Athavale *et al.*[13] also found a lower bleeding incidence in patients with impaired renal function with intravenous desmopressin.

A study by Rao *et al.*, which used intranasal desmopressin in patients with creatinine >1.5 mg/dL (excluding patients on dialysis), found a reduced risk of minor but not major complications consistent with our study.[14] This study had a near-universal incidence of hyponatremia in the desmopressin group, which was not seen in the current study. This may be because of the reduced antidiuretic effect of desmopressin due to the poorer renal function in our patients. However, as this was a retrospective study, information regarding mild cognitive dysfunction due to hyponatremia or a need for dialysis or ultrafiltration in case of fluid overload could not be ascertained accurately, and they were not specifically studied. As all patients in our study were inpatients, fluid intake is generally restricted in patients with significant renal failure, and a previous study shows that a single dose of desmopressin may not lead to hyponatremia unless concomitant excessive fluid intake was present.[15]

Desmopressin use did not decrease the incidence of major post-biopsy bleeding requiring a blood transfusion or a radiological intervention including gel foam embolization or coiling in the current study. This is in line with a large retrospective cohort study by Leclerc *et al.*,[16] who found similar rates of symptomatic hematomas and intervention in patients given desmopressin as those who did not receive desmopressin. A recent systematic review also found insufficient high-quality evidence to support the routine use of desmopressin before the biopsy.[17]

Therefore, the benefit of desmopressin in decreasing bleeding complications after renal biopsy seems restricted to minor hematomas or gross hematuria that resolve spontaneously and do not seem to extend to major complications that require transfusion or intervention. This may be due to the many variables that increase a patient's risk of bleeding, including age, gender, obesity, blood pressure, histological diagnosis, coagulation abnormalities, and poor technique that remain unaffected by desmopressin. When a patient had bleeding stemming from a pseudoaneurysm or an arteriovenous fistula, a correction of uremic hemostatic disorders by desmopressin may not be enough to contain the bleeding. These are possible reasons to explain the lack of benefit with desmopressin to prevent major bleeding complications.

The drawbacks of our study include its retrospective nature, single-center design, small numbers, and inclusion

of only patients with eGFR <30 mL/minute/1.73 m^2. The response to desmopressin was not measured in our study using bleeding time and platelet function analyzer, and a cost–benefit analysis was also not done.

Unlike many studies, our study has used intranasal desmopressin before renal biopsies, and whether the lack of benefit with desmopressin in reducing major complications is due to lower bioavailability needs to be studied. Therefore, further extensive, prospective studies are needed to clarify the optimal desmopressin route and dose and its complications including severe hyponatremia and thrombosis. Also, desmopressin nasal spray retails for more than INR 600 ($8) in India, and a cost–benefit analysis is needed before prescribing its routine use.

Conclusion

Intranasal desmopressin use in patients with eGFR <30 mL/minute/1.73 m^2 who underwent percutaneous renal biopsy was associated with a decrease in the overall rate of bleeding complications but did not decrease the rate of major bleeding episodes and need for intervention. The ideal dose and route of desmopressin and its role in patients across various stages of renal dysfunction are areas for future research.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Alwall N. Aspiration biopsy of the kidney 1: Including i.a. a report of a case of amyloidosis diagnosed through aspiration biopsy of the kidney in 1944 and investigated at an autopsy in 1950. Acta Med Scand 1952;143:430-5.
2. Kark R, Muehrcke R. Biopsy of kidney in prone position. Lancet 1954;263:1047-9.
3. Lees JS, McQuarrie EP, Mordi N, Geddes CC, Fox JG, Mackinnon B. Risk factors for bleeding complications after nephrologist-performed native renal biopsy. Clin Kidney J 2017;10:573-7.
4. Zhu MS, Chen JZ, Xu AP. Factors that can minimize bleeding complications after renal biopsy. Int Urol Nephrol 2014;46:1969-75.
5. Corapi KM, Chen JL, Balk EM, Gordon CE. Bleeding complications of native kidney biopsy: A systematic review and meta-analysis. Am J Kidney Dis 2012;60:62-73.
6. Nicholson ML, Wheatley TJ, Doughman TM, White SA, Morgan JD, Veitch PS, *et al*. A prospective randomized trial of three different sizes of core-cutting needle for renal transplant biopsy. Kidney Int 2000;58:390-5.
7. Mannucci PM. Desmopressin (DDAVP) in the treatment of bleeding disorders: The first 20 years. Blood 1997;90:2515-21.
8. Zeigler ZR, Megaludis A, Fraley DS. Desmopressin (d-DAVP) effects on platelet rheology and von Willebrand factor activities in uremia. Am J Hematol 1992;39:90-5.
9. Manno C, Bonifati C, Torres DD, Campobasso N, Schena FP. Desmopressin acetate in percutaneous ultrasound-guided kidney biopsy: A randomized controlled trial. Am J Kidney Dis 2011;57:850-5.
10. Peters B, Hadimeri H, Mölne J, Nasic S, Jensen G, Stegmayr B. Desmopressin (Octostim®) before a native kidney biopsy can reduce the risk for biopsy complications in patients with impaired renal function: A pilot study. Nephrology 2018;23:366-70.
11. Ozen S, Saatci U, Bakkaloglu A, Ozdemir S, Ozdemir O, Besbas N. Low-dose intranasal desmopressin (DDAVP) for uremic bleeding. Nephron 1997;75:119-20.
12. Radhakrishnan S, Chanchlani R, Connolly B, Langlois V. Pre-procedure desmopressin acetate to reduce bleeding in renal failure: Does it really work?. Nephron Clin Pract 2014;128:45-8.
13. Athavale A, Kulkarni H, Arslan CD, Hart P. Desmopressin and bleeding risk after percutaneous kidney biopsy. BMC Nephrol 2019;20:413.
14. Rao NS, Chandra A. Intranasal desmopressin reduces renal biopsy-related bleeding and serum sodium levels in patients with reduced renal function. Clin Kidney J 2019;13:1063-7.
15. Tsai SF, Chen CH, Shu KH, Cheng CH, Yu TM, Chuang YW, *et al*. Current safety of renal allograft biopsy with indication in adult recipients: An observational study. Medicine 2016;95:e2816.
16. Leclerc S, Nadeau-Fredette AC, Elftouh N, Lafrance JP, Pichette V, Laurin LP. Use of desmopressin prior to kidney biopsy in patients with high bleeding risk. Kidney Int Rep 2020;5:1180-7.
17. Lim CC, Tan HZ, Tan CS, Healy H, Choo J, Franca Gois PH. Desmopressin acetate to prevent bleeding in percutaneous kidney biopsy: A systematic review. Intern Med J 2021;51:571-9.